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Datasheet for the decision of 13 November 2013

Case Number: T 0061/10 - 3.3.07

Application Number: 97950300.0

Publication Number: 946143

IPC: A61K9/00

Language of the proceedings: EN

Title of invention:
A NITROIMIDAZOLE GEL COMPOSITION

Patent Proprietor:
Galderma S.A.

Opponent:
Dr.August Wolff GmbH & Co. Arzneimittel

Headword:

Relevant legal provisions:
EPC Art. 56

Keyword:
Main request and auxiliary requests 1 and 3, prohibition of reformatio in peius (yes)
Auxiliary request 2, inventive step (no)
Auxiliary request 4, admission into proceedings (no)

Decisions cited:
G 0001/99, T 1843/09, T 1979/11

Catchword:

In decisions G 1/99, T 1843/09 and T 1979/11 the existence of a causal link between the limiting feature to be deleted and the new situation arising on appeal was a necessary precondition for justifying an exception to the principle of prohibition of *reformatio in peius* for reasons of equity. As this precondition is not fulfilled in the present case, a departure from the principle of prohibition of *reformatio in peius* based on analogies with the cases underlying those decisions is not justified.

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Case Number: T 0061/10 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 13 November 2013

Appellant: (Opponent)	Dr.August Wolff GmbH & Co. Arzneimittel Sudbrackstrasse 56 33611 Bielefeld (DE)
Representative:	Grünecker, Kinkeldey, Stockmair & Schwanhäusser Leopoldstrasse 4 80802 München (DE)
Respondent: (Patent Proprietor)	Galderma S.A. Zugerstrasse 8 6330 Cham (CH)
Representative:	Macquet, Christophe Macquet & Associés Arche des Dolines 7, rue Soutrane 06560 Sophia Antipolis (FR)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 16 November 2009 concerning maintenance of the European Patent No. 946143 in amended form.**

Composition of the Board:

Chairman: D. Semino
Members: A. Usuelli
D. T. Keeling

Summary of Facts and Submissions

I. The appeal of the opponent (appellant) lies against the interlocutory decision of the opposition division announced at the oral proceedings on 20 October 2009 to maintain European patent N° 946143 in amended form.

The patent was granted with 30 claims. Independent claims 1 and 17 read as follows:

"1. A method of preparing a viscous hydrogel composition, for use in a topical treatment of a skin condition involving dry or inflamed skin, including a pharmaceutically active agent, a polysaccharide, a water—miscible organic solvent and water, comprising the steps of suspending the polysaccharide in the water-miscible organic solvent and mixing the resulting polysaccharide suspension into an aqueous medium, thereby to hydrate the polysaccharide and to form a viscous hydrogel composition, and adding the pharmaceutically active agent, wherein the pharmaceutically active agent is an antimicrobially active nitroimidazole drug, the water—miscible organic solvent is a water—miscible alkylelie *(sic)* glycol, and the composition is buffered to have a pH within the range of 4.5-6.5."

"17. A viscous hydrogel composition, for use in a topical treatment of a skin condition involving dry or inflamed skin, comprising an antimicrobially active nitroimidazole drug, a water-miscible alkylene glycol, a hydroxyalkyl cellulose gelling agent and water, buffered to have a pH within the range of 4.5—6.5 and wherein the water-miscible alkylene glycol is glycerol, dipropylene glycol, propylene glycol, butylene glycol,

pentylene glycol or hexylene glycol, and, preferably, propylene glycol."

II. An opposition was filed against the patent as a whole It was based on Article 100(a) together with Article 54 and 56 EPC and Article 100(c) together with Article 123(2) EPC. The opponent relied *inter alia* on the following documents:

D8: *Skin Pharmacology,* 1997; 10, pages 28-33
D9: Monthly Index of Medical Specialities, September 1994, page 250 and copy of packaging of Metrogel® Sandoz
D11: WO-A-92/16245
D13: Information concerning the marketing authorisation of Metrogel®
D14: Certificate of Analysis; Dr.Wolff
D20: Product Summary Metrogel®, Metronidazole BP 0.75%

III. The decision of the opposition division was based on the patent as granted as main request and on an auxiliary request filed during oral proceedings on 20 October 2009 and including a set of claims 1 to 15 and an amended description. The auxiliary request contained only process claims. Claim 1 of that request differed from claim 1 of the granted patent only in that it included the following sentence at the end of the claim:

"...wherein the nitroimidazole drug is dissolved in the aqueous medium, or suspended or dissolved in the water miscible organic solvent, before said suspension is mixed with said aqueous medium."

IV. In its decision, the opposition division came to the following conclusions:

a) The patent as granted met the requirements of Article 123(2) EPC.

b) Priority was not validly claimed as the skilled person could not unambiguously derive from the priority document that a hydrogel was necessarily obtained.

c) The subject-matter of product claim 17 was found to be novel over D8, D9 and D20 because none of these documents provided an unambiguous disclosure of a buffer within the range of pH 4,5-6,5. Starting from D8 as closest prior art, the problem to be solved by the product of claim 17 was seen in the avoidance of pH fluctuations. The use of a buffer was considered to be an obvious solution to this problem.

d) The process claims of the auxiliary request were considered inventive over the closest prior art D8, because the way of processing the ingredients in order to obtain an homogeneous gel was neither disclosed nor suggested therein.

V. The appellant lodged an appeal against that decision. With the statements of grounds the appellant submitted the following documents:

D21: Brochure Natrosol Hydroxyethylcellulose; Aqualon
D22: Brochure Blanose Cellulose gum; Aqualon
D23: Wikipedia extract: Puffer (Chemie)

VI. With the reply to the statement of grounds dated 15 October 2010 the patent proprietor (respondent) requested as main request the maintenance of the patent as granted and submitted three sets of claims as auxiliary requests 1 to 3.

Auxiliary request 1 contained 16 claims which were identical to claims 1 to 16 of the granted patent (i.e. the process claims).

Auxiliary request 2 comprised the same claims as the auxiliary request submitted during the opposition procedure and held allowable by the opposition division.

Auxiliary request 3 was identical to auxiliary request 1 with the addition in claim 1 of the step of "cooling the polysaccharide suspension" after the formation of the same.

VII. By its letter submitted on 9 November 2010, the appellant requested that the main request and auxiliary requests 1 and 3 be considered not admissible, on the ground that they violated the principle of *reformatio in peius*.

VIII. With letter of 4 September 2013 the respondent filed a further set of claims as auxiliary request 4. Auxiliary request 4 corresponded to auxiliary request 2 with the amendment of claim 1 introduced in auxiliary request 3.

IX. On 13 November 2013 oral proceedings were held before the Board.

X. As far as relevant to the present decision, the appellant's arguments can be summarized as follows:

a) The main request and auxiliary requests 1 and 3 were not to be admitted into the proceedings because their scope extended beyond the scope of the request held allowable by the opposition division, thereby contravening the principle of

prohibition of *reformatio in peius*. Only in exceptional circumstances is it possibile to deviate from the prohibition of *reformatio in peius* in order to give the patentee the possibility to react to new factual situations arising for the first time during the appeal procedure, if the consequence of these new situations would be for the patentee to lose any protection. However, such exceptional circumstances did not occur in present case. In this respect, the present case was not comparable with cases T 1843/09 (OJ EPO, 2013, 508) and T 1979/11 of 28 June 2013 (not published in the OJ), in which the Boards acknowledged the presence of exceptional circumstances.

b) With regard to the inventive step of the process claims, the closest prior art should be either document D8 or document D9. Both documents disclosed hydrogel compositions containing metronidazole as active ingredient and having a pH falling in the range 4.5-6.5. These compositions differed from the product obtained according to the process of the opposed patent only in that they did not contain a buffer. There were no experimental data showing that by the use of the claimed process it was possible to avoid the formation of clumps during the hydrogel manufacture. Furthermore, the addition of the buffer did not result in any other effect than the pH stabilization. It was evident from D23 that adding a buffer to stabilize the pH was part of the common general knowledge. The steps of the claimed process were based on conventional procedures. In particular, the preparation of a suspension of polysaccharide in a water miscible

organic solvent was disclosed in D11. A similar teaching was derivable also from D21 and D22. Accordingly, in the absence of any surprising effect the process was to be considered obvious.

c) Auxiliary request 4 should not be admitted since it was submitted at a very late stage of the procedure, well after the invitation to oral proceedings. Furthermore, the respondent did not provide any basis for the feature relating to the cooling of the polysaccharide suspension.

XI. As far as relevant to the present decision, the respondent's arguments can be summarized as follows:

a) The application of the principle of prohibition of *reformatio in peius* is subject to some exceptions. A first deviation from the application of this prohibition was established by the Enlarged Board of Appeal in the decision G 1/99 (OJ EPO, 2001, 381) in order to give the patentee the possibility to react to an objection under Article 123(2) arising from an amendment which was erroneously held allowable by the opposition division. Other exceptions to the application of the prohibition have been allowed in the decisions T 1843/09 and T 1979/11 (*supra*), in order to make it possible for the patentee to react to situations involving a change of the factual and/or legal basis of the decision on the opposition. A deviation from the application of the prohibition of *reformatio in peius* was justified also in the present case because the decision of the opposition division was based on an erroneous assessment of the validity of the priority claim. Furthermore, in view of the introduction of the new documents D21

to D23 and of the appellant's arguments based on these documents, the respondent was confronted for the first time in the appeal procedure with new objections concerning the inventiveness of the process claims. All requests were therefore to be admitted into the proceedings.

b) As to the inventive step of the process claims, D8 or D9 represented the closest state of the art. The hydrogel compositions disclosed in these documents did not contain any buffer. Furthermore, none of these documents provided information as to the process for their preparation. Examples 1 and 2 of the patent showed that the claimed process made the manufacture of homogeneous compositions possible. Accordingly, the problem of avoiding the formation of clumps had effectively been solved. Furthermore, example 13 provided experimental evidence of the possibility of using a hydrogel prepared according to the process of the invention in the treatment of rosacea. None of the cited documents suggested adding a buffer to the compositions disclosed in D8 or D9. The feature concerning the preparation of a suspension in a water-miscible organic solvent was also not suggested by the prior art documents. In this respect the skilled person would not take into account the teaching of D11 which related to the provision of gels having a different therapeutic application. Concerning the addition of the nitroimidazole drug, this could be added also after the formation of the hydrogels. The prior art did not suggest that the nitroimidazole drug was either to be dissolved in the aqueous medium or to be suspended in the organic solvent. For

these reasons, the presence of an inventive step had to be acknowledged.

c) Having regard to auxiliary request 4, the feature relating to the cooling of the polysaccharide suspension was included also in auxiliary request 3 which was submitted with the reply to the statements of grounds. Accordingly, auxiliary request 4 should be admitted into the procedure.

XII. The appellant requested that the decision be set aside and the patent be revoked.

XIII. The respondent requested the maintenance of the patent as granted or, in the alternative, the maintenance of the patent on the basis of one of auxiliary requests 1 to 3 filed with letter of 15 October 2010 or on the basis of auxiliary request 4 filed with letter of 4 September 2013.

Reasons for the Decision

1. *Main request and auxiliary request 1 - Reformatio in peius*

1.1 It is undisputed that the scope of claim 1 of both the main request and auxiliary request 1 is broader than the scope of claim 1 held allowable by the opposition division in view of the deletion of the limiting feature:

"...wherein the nitroimidazole drug is dissolved in the aqueous medium, or suspended or dissolved in the water miscible organic solvent, before said suspension is mixed with said aqueous medium.".

On this basis alone both requests run counter to the principle of prohibition of *reformatio in peius.* In order to decide on their admissibility, it is therefore necessary to establish whether compelling reasons exist for departing from the principle.

1.2 The respondent attempted to establish certain analogies between the present case and the cases underlying the decisions G 1/99, T 1843/09 and T 1979/11 (*supra*) in which departures from the principle of the prohibition of *reformatio in peius* were allowed.

1.2.1 The Enlarged Board of Appeal in G 1/99 considered it equitable, under certain circumstances, to deviate from the prohibition of *reformatio in peius* in order to give the opportunity to the patent proprietor to mitigate the effects of an error of judgement made by the opposition division that would have as a direct consequence the revocation of the patent. The error of judgment made by the opposition division was to allow an amendment which had the effect of limiting the scope of the claims and was objected to in appeal (see point 14 of the reasons).

1.2.2 In T 1843/09 (see point 2.4.4 of the reasons) and T 1979/11 (see point 2.1 of the reasons) it was held that the equitable approach taken by the Enlarged Board of Appeal in G 1/99 also covers situations involving a change of the factual or legal basis on which limitations have been made by the proprietor prior to the appeal.

1.2.3 In the case underlying decision T 1843/09 the limitation introduced during the opposition procedure was a feature having the effect of destroying the

validity of the priority. Following the admission during the appeal procedure of a highly relevant document published after the priority date, the patent proprietor was allowed to file a broader request in which the limiting feature not covered by the priority was deleted, thereby restoring the validity of the priority claim. Against this version of the claims, the post-published document admitted by the Board of Appeal could no longer be cited (see point 2.4.5 of the reasons).

1.2.4 In T 1979/11 the Board admitted the deletion of a limiting feature and by consequence a broadening of the scope of the claims vis-à-vis the version allowed by the opposition division, because this amendment was a reaction against an objection under Article 83 EPC which was raised for the first time in the statement of the grounds of appeal.

1.3 In contrast to the opinion expressed by the respondent, the Board considers that neither a possible error of judgment in the validity of the priority claim, nor the filing of documents D21 to D23 with the statement of grounds can render the situation in the present case similar to the one in the cited decisions.

1.4 In the cases underlying all cited decisions a causal link existed between the limiting feature to be deleted and the new situation arising in appeal procedure. In the case underlying G1/99 an error of judgment of the opposition division in allowing the addition of the limiting feature was objected to during the appeal procedure. In T 1843/09 the addition of the limiting feature had the effect of destroying the validity of the priority with the consequence that a post-published document became highly relevant. Finally, in the case

underlying T 1979/11 an issue of sufficiency was related to the limiting feature.

1.5 In the present case, the priority issue is related to the definition of the composition produced by the method of the invention as a hydrogel, which issue is equally relevant for process claim 1 of the main request and of auxiliary request 1 independently of the limiting feature. Similarly, documents D21 to D23 were cited by the appellant to reinforce an inventive step objection based on document D8 as closest prior art which is equally valid for a method of production with or without the limiting feature.

1.6 The present Board is of the opinion that in the cited decisions the existence of a causal link between the limiting feature to be deleted and the new situation arising on appeal was a necessary precondition for justifying an exception to the principle of prohibition of *reformatio in peius* for reasons of equity.

1.7 As this precondition is not fulfilled in the present case, a departure from the principle of prohibition of *reformatio in peius* based on analogies with the cases underlying decisions G 1/99, T 1843/09 and T 1979/11 (*supra*) is not justified. Other reasons for departing from the principle are not present nor have been invoked by the respondent.

1.8 In view of the above, the main request and auxiliary request 1 are not admitted into the procedure.

2. *Auxiliary Request 2 - Inventive Step*

2.1 The subject-matter of claim 1 relates to a process for preparing a viscous hydrogel composition for use in the

topical treatment of dry or inflamed skin, and containing as active agent an antimicrobially active nitroimidazole drug such as metronidazole. In the patent in suit, it is explained that an inconvenience that can be encountered in the preparation of gels containing metronidazole, is the formation of insoluble clumps which in turn may result in broad pH fluctuations of the final product (see paragraph [0005]). The process of the patent aims at the provision of a process solving these problems (see paragraph [0008]).

2.2 In agreement with the opposition division and with the approach followed by the parties at the oral proceedings, the Board considers D9 as the closest prior art.

2.2.1 D9 includes a copy of the packaging of the medicament Metrogel®. This document contains *inter alia* information concerning the Batch Number of the medicament (BN 4519) and the expiration date (06/95). The latter information is evidence that the product Metrogel® was marketed before the priority date of the patent, which was not contested by the respondent.

2.2.2 The parties agreed that the composition of Metrogel®, as disclosed in D9, differs from the composition of the hydrogel prepared in accordance with claim 1 only in that it does not contain a buffer to stabilize the pH in the range of 4.5-6.5. In addition, the certificate of analysis D14, submitted by the appellant, shows that the product Metrogel® with Batch Number 4519 has intrinsically a pH of 4.97, i.e. a pH falling in the range of 4.5-6.5.

2.2.3 Although D9 is evidence that the product Metrogel® was available before the priority date and was therefore also prepared before that date, this document does not provide any information as to the method used for preparing the product.

2.3 The technical problem as set out in the description of the present invention may be seen in the provision of a process for preparing a nitroimidazole based hydrogel composition which allows clumping to be avoided so that the compositions can be produced consistently and within an acceptable narrow pH range (see paragraph [0014]).

2.3.1 It must therefore be investigated whether there is sufficient evidence showing that this technical problem is solved with respect to the disclosure of D9.

2.3.2 Examples 1 and 2 of the patent disclose two alternative methods according to claim 1, for preparing a hydrogel composition containing 0.75% of metronidazole. The two methods basically differ in that in example 1 the metronidazole is dissolved in the aqueous solution while in example 2 it is added to the organic solvent to form a suspension. According to both examples, the mixture obtained at the end of the procedure is defined as homogeneous. The Board regards these two examples as a sufficient evidence supporting the effect of avoiding the formation of clumps. On the other hand no evidence is available to show that this effect represents an improvement with respect to the product of D9. Without evidence in this respect, the Board can only assume that the product of D9, which is commercially available, is also an homogeneous product which does not contain clumps.

2.3.3 The patent specification does not contain any experimental data concerning the pH stability. It is however explained in the description, that the pH fluctuations are a consequence of the clumps formation ([0005] and [0014]). Furthermore, the hydrogel compositions of the invention contain a buffer. Accordingly, the Board sees no reasons for doubting the fact that the final compositions can be produced within an acceptable narrow pH range. In addition, due to the presence of a buffer, pH fluctuations are clearly avoided. As to the product of D9, while the evidence on file clearly shows that a value of the pH in the desired range is obtained, the absence of a buffer suggests that pH fluctuations occurring for instance during storage or after skin contact as described in the patent (see paragraph [0016]) cannot be avoided.

2.3.4 The experimental results disclosed in example 13 of the patent showing the efficacy of the metronidazole gel in the treatment of patients suffering from *rosacea*, which were cited additionally by the respondent in support of an inventive step, have no relevance for the formulation of the technical problem, as these data do not permit any inference as to the impact of the process claimed on the pharmacological properties of the hydrogels.

2.3.5 The technical problem effectively solved with respect to D9 is therefore the provision of a process for preparing a nitroimidazole based hydrogel composition without clumps as the one of D9 in which additionally pH fluctuations are avoided.

2.4 The question to be answered is whether the proposed solution would have been obvious to a skilled person in the light of the prior art.

2.4.1 As explained above, the composition of D9 differs from the hydrogel obtained according to the process of the opposed patent, only in that it does not contain a buffer. Accordingly, in order to answer the question above, it must be verified whether the addition of a buffer into the composition of D9 and the steps of processing the ingredients as defined in claim 1, are obvious in view of the prior art documents. According to the wording of claim 1, the processing steps are the following:

a) suspending the polysaccharide in the water-miscible organic solvent and mixing the resulting polysaccharide suspension into an aqueous medium, thereby to hydrate the polysaccharide and to form a viscous hydrogel composition, wherein the water—miscible organic solvent is a water—miscible alkylene glycol;

b) adding an antimicrobially active nitroimidazole drug, wherein the nitroimidazole drug is dissolved in the aqueous medium, or suspended or dissolved in the water miscible organic solvent, before said suspension is mixed with said aqueous medium.

2.4.2 Document D11 which discloses a wound dressing containing a cellulose derivative, water and a polyol component in the form of a gel (see claim 1), suggests step a). According to the teaching of this document, the gel can be prepared in a process comprising a first step of blending a cellulose derivative with a polyol (page 15, lines 3-7 and claim 23). This procedure is applied in examples 1 to 3 of D11 (pages 18 to 22). In example 1, cross-linked carboxymethyl cellulose is added to monopropylene glycol to form a slurry. The slurry is then added to an aqueous medium and mixed to

form a gel. There is no indication in D11 that this procedure may result in the formation of clumps. On the contrary, it is affirmed in example 1 that the addition of the cellulose derivative in the organic solvent can be carried out ensuring that no lump formation occurs. Furthermore, as for the examples of the opposed patent, the gel obtained according to D11 is defined as homogeneous (page 14, line 14; page 15, line 7).

2.4.3 The argument of the respondent that the skilled person would not consider the teaching of D11, as it relates to gels having a different therapeutic application, is not convincing. The opposed patent addresses the problem of overcoming certain technical difficulties that may arise during the preparation of a hydrogel. The focus of the invention is therefore on aspects of pharmaceutical technology rather than pharmacology. Accordingly, the skilled person aiming at the solution of the problems posed by the preparation of hydrogels would have no reason to confine himself to considering only documents concerning medicaments having the same therapeutic application as the hydrogels of the invention.

2.4.4 It follows from the above that before the priority date the skilled person was already aware that the formation of clumps could be avoided if the polysaccharide was suspended in an organic solvent and then mixed with the aqueous medium.

2.4.5 D11 does not give any information whether the procedure of suspending the polysaccharide in an organic solvent and mixing the suspension with an aqueous medium may have an impact on the pH stability. Having regard to the fact that pH fluctuations are a consequence of the clumps formation, the Board considers that the skilled

person would regard the procedure suggested in D11 as compatible also with the aim of keeping pH under control.

2.4.6 Step b), merely indicates that the active ingredient is added, either to the aqueous medium or to the organic solvent, but it cannot be added after the two liquid systems have been mixed to form the hydrogel. In other words, this feature has the effect of excluding one of the three possibilities for introducing the active ingredient in the final composition. There is however no evidence that this choice results in some unexpected effect. The Board considers therefore that this selection of two out of three equally possible alternatives does not contribute to the inventiveness of the process.

2.4.7 It remains to be verified whether the addition of a buffer into the composition of D9 would be evident for a skilled person aiming at solving the posed problem. In this respect it must be observed that the claim neither identifies the buffer, nor indicates at which stage of the procedure the buffer is introduced into the composition. Furthermore, there is no evidence that the addition of the buffer results in some effect different from the one of stabilizing of the pH. In particular, there are no data suggesting that the buffer may have a beneficial effect in avoiding clumps formation. Since the normal function of a buffer is exactly the one for which it is used in the hydrogel of the invention, namely maintaining the acidity near to a certain value, the Board sees no inventive contribution deriving from the feature of buffering the composition within the range 4.5-6.5.

2.5 Having regard to the reasons given above, the Board considers that the subject-matter of claim 1 of the second auxiliary request does not involve an inventive step.

3. Auxiliary Request 3

3.1 Claim 1 of this request does not include the feature requiring the nitroimidazole drug to be dissolved in the aqueous medium or suspended or dissolved in the organic solvent and therefore contravenes the principle of *reformatio in peius f*or the same reasons as claim 1 of the main request and auxiliary request 1.

3.2 The respondent argued in favour of the admissibility of this request with the same arguments submitted in respect to the main request and auxiliary request 1.

3.3 It follows that auxiliary request 3 is inadmissible for the same reasons as given for the main request and auxiliary request 1 (point 1 above).

4. *Auxiliary request 4*

4.1 This request was submitted on 4 September 2013, i.e when oral proceedings had already been arranged. The respondent did not provide any justification for the late filing of the request. In addition, no basis was indicated for the added feature and no reasons were given to explain how that feature could address the issue of lack of inventive step.

4.2 The Board does not see any justification for the late filing, as the concerns regarding admissibility of the main requests and of auxiliary requests 1 and 3 had been on file for almost three years (see letter of the

appellant dated 9 November 2010). In addition to the doubts concerning the compliance with the requirements of Article 123(2) EPC, it is also not apparent for the Board how the amendments introduced in auxiliary request 4 could overcome the objection under Article 56 EPC.

4.3 In view of this, the Board considers it appropriate to exercise its discretion under Article 13 of the Rules of Procedure of the Boards of Appeal by not admitting auxiliary request 4 into the proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside

2. The patent is revoked.

The Registrar: The Chairman:

S. Fabiani D. Semino

Decision electronically authenticated